REMARKS

Claims 1, 3-26, and 75-82 were pending in this application. Claim 77 has been amended. Accordingly, claims 1, 3-26, and 75-82 will remain pending in the application.

Support for the amendment to claim 77 may be found throughout the specification and in the claims as originally filed.

No new matter has been added. Amendment of the claims should in no way be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or one or more separate applications.

Allowable Subject Matter

Applicants gratefully acknowledge the Examiner's indication that claims 1 and 75-76 are allowable.

Withdrawal of Certain Objections and Rejections

Applicants gratefully acknowledge the Examiner's indication that the objection of claims 3, 7, 9, 17, 21, 24, 25, and 26 and the rejection of claim 1 under 35 U.S.C. §102(b), as set forth in the Office Action dated June 3, 2003, have been withdrawn.

Rejection of Claims 3-7, 9-10, 13-15, 17-26 and 77 Under 35 U.S.C. §102(b)

The Examiner has maintained the rejection of claims 3-7, 9-10, 13-15, 17-26, and has further rejected claim 77 under 35 U.S.C. §102(b) as being anticipated by Pearson *et al.* (*J. of Bacteriol* (1997) 179(18): 5756-5767) "for reasons already of record." In particular, the Examiner is of the opinion that

> [t]he rejection was on the grounds that Pearson et al., teach a method for identifying a modulator of quorum sensing signaling in bacteria, comprising the claimed steps. Applicants assert that Pearson et al., does not teach that the test compound is other than the quorum sensing signal molecule. In response to applicant's argument that the Pearson et al. reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the test compound is other than the quorum sensing signal molecule) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns,* 988 F.2d 1181, 26 USPQ2d

> 1057 (Fed. Cir. 1993). It is noted that new independent claim 77 does not require that the test compound is other than the quorum sensing signal molecule. Claims 3-7, 9-10, 13-15, 17-26 and 77 all recite alternative language to embrace claim 77. Therefore, applicants' arguments are not found persuasive . . . . It is also noted that that the claims only requires a cell which is capable of endogenously synthesizing a quorum sensing signal, therefore, the cell does not have to actually synthesize a quorum sensing signal. Furthermore, Pearson et al., teach several cells which would be capable of endogenously producing a quorum sensing signal.

Applicants respectfully traverse the foregoing rejection under 35 U.S.C. §102(b) for the reasons set forth in the Preliminary Amendment filed on December 3, 2003, and for the following reasons.

Pearson *et al.* investigates the roles of the *rhl* and *las* quorum sensing systems in the expression of certain virulence genes, *e.g.,* the rhamnolipid biosynthesis operon *rhlAB* and *lasB.* Pearson *et al.* describes the use of mutant strains of bacteria, including mutant strains of *Pseudomonas aeruginosa*, which are unable to produce a quorum sensing signal molecule. The mutant strains contain a reporter gene and a transcriptional activator. PAI-1 and PAI-2, the quorum sensing signal molecules (which are the endogenously produced autoinducers of *las* and *rhl* systems in *Pseudomonas aeruginosa*), were exogenously added and the reporter gene was monitored. Pearson *et al.* showed that PAI-2, the quorum sensing signal molecule, is required for expression of *rhlAB*, and that PAI-2 interacts with RhlR to induce *rhlA* expression. Pearson *et al* also teach that PAI-1 does not significantly activate RhlR to induce either *rhlA* or *lasB* expression, indicating that RhlR has high specificity for its cognate autoinducer, PAI-2 (see page 5762, last two paragraphs of second column and first paragraph of page 5763, and page 5765, first paragraph).

Claim 77 is directed to a method for identifying a modulator of quorum sensing signaling in bacteria, said method comprising: providing a cell which comprises a regulatory sequence of a quorum sensing controlled gene operatively linked to a gene that generates a detectable signal in response to a quorum sensing signal molecule; ***contacting said cell with said quorum sensing signal molecule in the presence and absence of a test compound***; and detecting a change in said detectable signal to thereby identify said test compound as a modulator of quorum sensing signaling in bacteria.

As the Examiner is well aware, for a prior art reference to anticipate a claimed invention, the prior art must teach ***each and every element*** of the claimed invention. Lewmar Marine v. Barient, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Applicants respectfully submit that Pearson *et al.* fail to teach each and every limitation of claim 77. The main focus of the Pearson *et al.* reference is to characterize the quorum sensing signaling pathway including the roles of the *rhl* and *las* quorum sensing systems in the expression of certain virulence genes. Pearson *et al.* study the expression of genes in the presence of certain quorum sensing signaling molecules (*e.g.*, PAI-2).

The presently claimed invention is directed to methods for identifying a modulator of quorum sensing signaling in bacteria comprising providing a cell which comprises a regulatory sequence of a quorum sensing controlled gene operatively linked to a gene that generates a detectable signal in response to a quorum sensing signal molecule; ***contacting said cell with said quorum sensing signal molecule in the presence and absence of a test compound***. The Examiner is of the opinion that claim 77 does not require that the test compound be other than the quorum sensing signal molecule. However, the phrase ***"contacting said cell with said quorum sensing signal molecule in the presence and absence of a test compound"*** refers to both a quorum sensing signal molecule and a test compound. Therefore, the test compound must be a compound other than the quorum sensing signal molecule. The pending claims require that, ***in addition*** to the quorum sensing signal molecule, a test compound is added. Pearson *et al.* do not teach or suggest contacting a cell with ***both*** a quorum sensing signal molecule ***and*** a test compound, in order to identify modulators of quorum sensing signaling. Furthermore, Pearson *et al.* do not teach or suggest the use of ***any*** test compound other than a quorum sensing signal molecule to identify a modulator of quorum sensing signaling. Thus, Pearson *et al.* do not teach or suggest each and every element of the claimed invention.

The Examiner is further of the opinion that

> [i]n response to applicant's arguments that Pearson et al., does not teach an assay to identify a modulator of quorum sensing signaling, the recitation of a method to identify a modulator of quorum sensing signaling has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao,*

> 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie,* 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicants respectfully submit that Pearson *et al.* do not teach or suggest a screening assay to identify a modulator of quorum sensing signaling in bacteria as is claimed in claim 77. With respect to the use of terms in the preamble, the M.P.E.P. states that "[a] claim preamble has the import that the claim as a whole suggests for it" (M.P.E.P. 2111.02; Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995)). The M.P.E.P. further states that "[i]f the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is `necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." (M.P.E.P. 2111.02; Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951)). Therefore, the preamble of a claim may be given patentable weight. The preamble of claim 77 is "necessary to give life, meaning, and vitality" to the claim, and therefore should be given patentable weight. Therefore, because Pearson *et al.* fail to teach or suggest a method for identifying a modulator of quorum sensing signaling in bacteria, comprising contacting a cell with a quorum sensing signal molecule in the presence and absence of a test compound to detect a change in a detectable signal, Pearson, *et al.* fail to teach or suggest each and every element of claim 77.

Accordingly, for the reasons set forth above, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection under 35 U.S.C. §102(b).

Rejection of Claims 8, 11-12, and 16 Under 35 U.S.C. §103(a)

The Examiner has maintained the rejection of claims 8, 11-12, and 16 under 35 U.S.C. §103(a) as being unpatentable over Pearson *et al.* (*J. of Bacteriol.* (1997) 179(18): 5756-5767) in view of Passador *et al.* (*Science*, 1993. 260:1127-1130) "for reasons already of record." In particular, the Examiner is of the opinion that

> it would have been prima facie obvious at the time of applicants invention to modify the method for identifying a modulator of quorum sensing signaling in bacteria comprising the recited steps as taught by Pearson et al., to include a second cell that produces the quorum sensing signal molecule, instead of adding the molecule to the cell. Applicants assert that the contact step wherein

> the cell is contacted in the presence and absence of the test compound distinguishes the claims from the prior art. However, Pearson et al., teach controls which thereby meet the limitations of the claims with regard to the contact step. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones,* 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have a reasonable expectation of success in using a second cell to produce the molecule since Passador et al., teach that the expression of *P. aeruginosa* virulence genes requires cell-to-cell communication whereby one cell produces the molecule and the other cell can respond to the production of the molecule.

Applicants respectfully traverse the foregoing rejection for the following reasons. To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.,* 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, *e.g., Carella v. Starlight Archery,* 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985). ***Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations*** (M.P.E.P. 2143).

Claim 77 is directed to a method for identifying a modulator of quorum sensing signaling in bacteria comprising providing a cell which comprises a regulatory sequence of a quorum

sensing controlled gene operatively linked to a gene that generates a detectable signal in response to a quorum sensing signal molecule; ***contacting said cell with said quorum sensing signal molecule in the presence and absence of a test compound***; and detecting a change in said detectable signal to thereby identify said test compound as a modulator of quorum sensing signaling in bacteria.

As set forth above, the primary reference of Pearson *et al.* fails to teach or suggest a method for identifying a modulator of quorum sensing signaling in bacteria comprising ***contacting said cell with said quorum sensing signal molecule in the presence and absence of a test compound***, as is required by claim 77, and claims depending therefrom, including claims 8, 11-12, and 16. Pearson *et al.* do not teach or suggest contacting a cell with ***both*** a quorum sensing signal molecule ***and*** a test compound, in order to identify modulators of quorum sensing signaling.

Moreover, the secondary reference of Passador *et al.* fails to cure the deficiencies in the teachings of the Pearson *et al.* reference. Passador describes that *Pseudomonas autoinducer* (PAI) provides *P. aeruginosa* with a means of cell-to-cell communication that is required for expression of virulence genes and that PAI may provide a target for therapeutic approaches. Passador *et al.* does not teach or suggest a method for identifying a modulator of quorum sensing signaling in bacteria comprising contacting said cell with a quorum sensing signal molecule ***in the presence and absence of a test compound***, as is required by claim 77 and claims depending therefrom, including claims 8, 11-12, and 16.

In view of the foregoing, Applicants respectfully submit that the combination of Pearson *et al.* and Passador *et al.* fail to teach or suggest Applicants' invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw rejection of the pending claims under 35 U.S.C. §103.

Rejection of Claims 5 and 6 Under 35 U.S.C. §112, Second Paragraph

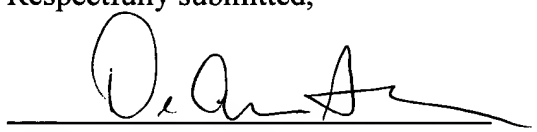
Claims 5 and 6 are rejected under 35 U.S.C. §112, second paragraph, as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[t]he acronyms in the claims must be spelled out when used for the first time in a chain of claims."

Applicants respectfully traverse the foregoing rejection. Applicants respectfully point out that the terms listed in claims 5 and 6 are not acronyms. Rather, these are gene names which are well-known in the art and widely acceptable as identifiers of specific genes. Acronyms are abbreviations which are formed from the initial letters of groups of words. The letters of these gene names do not represent the first letters of words, and therefore, cannot be "spelled out." Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

SUMMARY

In view of the above remarks and the amendments to the claims, it is believed that this application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



DeAnn F. Smith, Esq.
Reg. No.: 36,683
Attorney for Applicants

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

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